authors conclude that the combination of vitamin K antagonists (VKA) and clopidogrel may serve as a valuable alternative to a triple antithrombotic regimen also including aspirin, based on the results of 1 small randomized controlled trial and a large nationwide registry (2,3).

In a recent joint consensus document from multiple European Associations, endorsed by the Heart Rhythm Society and Asia-Pacific Heart Rhythm Society, dual therapy consisting of VKA and clopidogrel "may" (i.e., Class IIb) or even "should" (i.e., Class IIa) be considered in patients with stable coronary artery disease undergoing stenting with variable lengths and strengths of recommendation depending on individual stroke (i.e., CHA_2DS_2-VASc score = 1 or ≥2) and bleeding (i.e., HAS-BLED = 0 to 2 or ≥3) risks (4). We underscore that aspirin should not be dropped in patients at low bleeding risk on long-term VKA therapy in the context of an acute coronary syndrome (ACS)—with or without stenting, and for at least the first 6 months—because: 1) the benefit of dual antiplatelet therapy in ACS patients is established (5); and 2) the WOEST (What is the Optimal antiplatElet and anticoagulant therapy in patients with oral anticoagulation and coronary StenTing) trial included only a minority (~25%) of patients with an ACS (2). Other limitations of the WOEST trial are also evident, including the prolonged period (12 months) of triple therapy and the endpoint driven by minor bleeds (with major bleeds not different between triple and dual therapy) (4).

In the Danish registry, where only ACS patients where included by study design, the adjusted risk of all-cause mortality compared with aspirin monotherapy was numerically, albeit not significantly, lower with triple antithrombotic therapy (i.e., hazard ratio: 1.04) than with a dual therapy regimen of VKA and clopidogrel (i.e., hazard ratio 1.22), whereas the risk of fatal and nonfatal bleeding was significantly increased with both regimens (3). As far as the duration of triple antithrombotic therapy is concerned, the joint European document points out that the period where maximum antithrombotic protection should be given (in patients at low or moderate bleeding risk) corresponds to the first 6 months after the onset of an ACS and/or a second-generation drug-eluting stent implantation (4). This has been recently found to be consistent with the 2014 European guidelines for myocardial revascularization (5) and the newly presented ISAR-TRIPLE (Intracoronary Stenting and Antithrombotic Regimen–Testing of a six-week versus a six-month clopidogrel treatment Regimen In Patients with concomitant aspirin and oraL anticoagulant therapy following drug-Eluting stenting) study (presented at Transcatheter Cardiovascular Therapeutics, September 2014, Washington, DC).

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Please note: Drs. Capodanno and Lip are coauthors of a recent joint consensus document from multiple European Associations, endorsed by the Heart Rhythm Society and Asia-Pacific Heart Rhythm Society. Dr. Capodanno receives speaker's honoraria from Bayer, AstraZeneca, Eli Lilly and Company/Daiichi-Sankyo, Abbott Vascular, and Stentys.

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REPLY: Triple Therapy for Atrial Fibrillation and ACS With or Without PCI

Don't Drop Aspirin Just Yet

We thank Drs. Capodanno and Lip for their interest in and valuable comments on our recent review (1) on triple therapy for atrial fibrillation (AF) and percutaneous coronary intervention (PCI).

The conclusion of our review was that it might be a reasonable option to treat with a combination of vitamin K antagonists (VKA) and clopidogrel, which

is the only combination having shown favorable results compared with triple therapy (TT), based on the results of a randomized trial and a nationwide registry (1).

Drs. Capodanno and Lip highlight the recent guideline and consensus documents from multiple European associations (2,3) and state that aspirin should not be dropped in patients with low bleeding risk and acute coronary syndrome (ACS). We acknowledge the great work done by the authors of both guidelines and this consensus document (2,3). Of course, we recognize the limitations of the WOEST (What is the Optimal antiplatElet and anticoagulant therapy in patients with oral anticoagulation and coronary StenTing) trial (only one-quarter of patients with ACS) and the Danish registry, and these limitations were extensively described in our recently published review (1,4,5). On the other hand, the Class IIA recommendation in the European consensus and guidelines to use TT in patients with AF and PCI is made on a Level of Evidence: C, which is "consensus of opinion of the experts and/or small studies, retrospective studies, registries." Unfortunately, there is not one randomised trial favoring TT.

Furthermore, Drs. Capodanno and Lip state that the number of major bleeding events in the WOEST trial did not differ. Again, we recognize the limitations of the WOEST trial in that most bleedings prevented were minor and minimal. However, Capodanno and Lip's statement is not completely true. Although there was no significant difference in Thrombolysis In Myocardial Infarction major bleeding events, there was, however, a significant difference in the newer, but widely accepted, Bleeding Academic Research Consortium 3 bleeding classification, which corresponds with major bleeding (1,4).

Moreover, the Danish registry containing 12,000 patients provides sufficient power to state that the combination of VKA and clopidogrel is safe with regard to thrombotic and thromboembolic complications such as myocardial infarction and ischemic stroke, which was a major concern because of the lack of power regarding the ischemic endpoints in the WOEST trial (1,5).

In patients with AF and ACS, our conclusion was backed up by the recently presented AVIATOR registry containing 859 patients, which also showed fewer bleeding events in patients without aspirin, whereas no difference in the ischemic endpoints was observed in patients treated with dual therapy as compared with TT (presented at Transcatheter Cardiovascular Therapeutics, September 2014, Washington, DC).

Finally, the authors attract attention to the results of the ISAR-TRIPLE (Intracoronary Stenting and Antithrombotic Regimen-Testing of a six-week versus a six-month clopidogrel treatment Regimen In Patients with concomitant aspirin and oraL anticoagulant therapy following drug-Eluting stenting) trial (presented at Transcatheter Cardiovascular Therapeutics, September 2014, Washington, DC). However, the design of this trial was vitally different from the WOEST trial because aspirin was continued in ISAR-TRIPLE, whereas aspirin was stopped in WOEST with the aim to reduce bleeding events. Additionally, clopidogrel was stopped early after stenting in ISAR-TRIPLE to reduce bleeding, whereas previous publications show clopidogrel to be essential in preventing stent thrombosis. The hypothesis of the WOEST trial was that clopidogrel needed to be continued to adequately prevent stent thrombosis (1,5).

In conclusion, we agree with Drs. Capodanno and Lip that the burden of evidence favoring the combination VKA + clopidogrel is still limited; on the other hand, we also have to acknowledge the fact that there is not one randomized trial favoring TT. Therefore, we will have to wait for the results of the large ongoing randomized trials, such as the PIONEER AF (A Study Exploring Two Strategies of Rivaroxaban and One of Oral Vitamin K Antagonist in Patients With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention) and RE-DUAL PCI (Evaluation of Dual Therapy With Dabigatran vs. Triple Therapy With Warfarin in Patients With AF That Undergo a PCI With Stenting) trials.

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